REMARKS

Claims 1-4 and 19 are pending and rejected.

Claims 5-18 and 20-52 were withdrawn from consideration as directed to non-elected inventions.

The specification has been amended to remove the priority claim and also to add a sequence identifier.

The Sequence Listing has been amended update the priority claim and to incorporate a sequence disclosed on page 43 of the application as originally filed. New SEQ ID NO:37 represents the C-terminal most 466 amino acids of SEQ ID NO:2. Applicants attach hereto a paper copy and computer readable form of the updated Sequence Listing along with a Statement to Support.

Claims 1-4 have been amended. Claim 1 was amended to recite a specific SEQ ID NO. Claim 2 was amended to clarify that the claimed human RNase III polypeptide cleaved double-stranded RNA. Claim 3 was rewritten in independent form and was amended to clarify that the claimed human RNase III polypeptide cleaved double-stranded RNA. Claim 4 was amended to specify that the claimed human RNase III polypeptide cleaves double-stranded RNA and that the polypeptide comprises an amino acid sequence which is at least 90% homologous to SEQ ID NO:2. Support for the amendments can be found throughout the application as filed, especially on pages 29-30 and 32-33, and in Examples 9 and 10 on pages 43-44.

New claim 53 has been added. New claim 53 recites a composition comprising a human RNase III polypeptide which cleaves double-stranded RNA wherein the polypeptide comprises an amino acid sequence which is at least 90% homologous to SEQ ID NO:37, and a pharmaceutically acceptable carrier. Support for new claim 53 can be found throughout the application as filed, especially on pages 29-30 and 32-33, and in Examples 9 and 10 on pages 43-44. Applicants respectfully assert that the entry of new claim 53 will not necessitate a further search because SEQ ID NO:37 merely presents a fragment of SEQ ID NO:2, a sequence previously searched by the Office.

No new matter has been added via the foregoing amendments.

Upon entry of this amendment, claims 1-4, 19, and 53 will be pending.

Preliminarily, Applicants wish to thank the Examiner for the courtesies extended during a teleconference with the undersigned on July 21, 2003. Applicants have made claim amendments consistent with the comments and suggestions offered by the Examiner.

Priority

Applicants note the Examiner's statement that "[t]he claimed invention (claims 1-4 and 19) is awarded a priority date of, 07/06/01, the filing date of the instant application." (Office Action, page 2). Accordingly, Applicants have amended the specification to remove the priority claim. Applicants attach hereto a request for a corrected Filing Receipt along with an Unexecuted Oath/Declaration, both reflecting the removal of the priority claim. Applicants will file an Executed Oath/Declaration under separate cover.

Information Disclosure Statement

As noted in Applicants "Response" to Office Action mailed April 16, 2003, reference AD (Elbashir *et al.*, Nature 2001 15:188-200) was not initialed on the Form 1449 returned by the Examiner attached to the Office Action dated December 16, 2002 (paper no. 14). Applicants enclose for the Office's convenience a copy of the Elbashir reference as well as a copy of the otherwise initialed Form PTO 1449. Applicants respectfully request consideration of the Elbashir reference.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 4 and 19 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. Applicants respectfully disagree because the specification sufficiently describes the claimed subject matter.

The Office indicates that:

> the claims [claims 1, 2, 4 and 19] fail to provide a structure that would be correlated with a function. Claims 1, 4 and 19 provide for structures unrelated to SEQ ID NO:2 and more specifically other than that structure, the 466 C-terminal-most amino acids of SEQ ID NO:2 that provides for the function of double stranded RNA cleavage and claim 2 fails to provide for a function that would correlate with a recited structure (e.g. 90% identity but

> with any function that may or may not have been correlated in the art or instant specification with such a structure, for example).

(Final Rejection, page 6).

Although Applicants disagree, solely in an attempt to advance the pending claims to issuance, Applicants have amended claims 1-4 and have added new claim 53. Each pending claim recites a structure with a correlated function.

Claim 1, amended herein, provides a structure, SEQ ID NO:37, with a correlated function, cleaving double-stranded RNA.

Claim 2, amended herein, provides a structure, at least 90% homology to SEQ ID NO: 2, with a correlated function, cleaving double-stranded RNA.

Claim 3, amended herein, provides a structure, SEQ ID NO: 2, with a correlated function, cleaving double-stranded RNA.

Claim 4, amended herein, provides a structure, at least 90% homology to SEQ ID NO: 2, with a correlated function, cleaving double-stranded RNA.

New claim 53 provides a structure, at least 90% homology to SEQ ID NO:37, and a function, cleaving double-stranded RNA.

Applicants respectfully assert that one of skill in the art would readily acknowledge that the application as filed provides ample written description for claims 1-4, 19 and 53.

The application as filed provides nucleotide and amino acid sequences for human RNase III (see SEQ ID NOS:1 and 2, respectively), as well as the amino acid sequence for the RNase III domain of SEQ ID NO:2 (SEQ ID NO:37). As acknowledged by the Examiner, the application also sets forth methods for identifying RNase III polypeptides which cleave double-stranded RNA (*see*, for example, Example 10).

Applicants respectfully assert that the genera of proteins claimed comply with the written description requirement. For example, Applicants provide representative species of the genus. There is actual reduction to practice of both SEQ ID NO:2 and SEQ ID NO:37. As discussed above, the pending claims all recite both structure and function. In the pending claims which recite a genus, there is no substantial variation between species since all of the species within the genus must have at least 90% identity to a recited SEQ ID NO. Applicants provide a stated degree of homology (90%) which imposes a

structural relationship between members of the genus. Applicants' specification also teaches methods for determining whether a polypeptide cleaves double-stranded RNA.

The Office Action has failed to provide any evidence or reasoning why the specific species described, along with a description of the structure and function of the human RNase III that comprise the claimed genera, does not constitute adequate description of the claimed subject matter. One of skill in the art would conclude that Applicants were in possession of the necessary common attributes possessed by the members of the genus and that the disclosure meets the requirements of 35 USC §112, first paragraph, as providing adequate written description for the claimed invention.

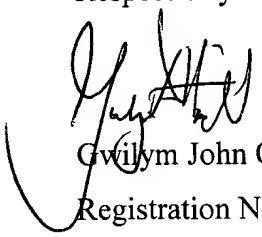
Applicants respectfully assert that the Office has misinterpreted the teaching of the Wu reference (Wu *et al.*, J. Biol. Chem, Vol. 275, No. 47, 36957-36965, **2000**). The Wu reference does ***not*** suggest that "the species specifically disclosed [in the present application] are not representative of the genus because the genus is highly variant . . ." (Final Rejection, page 4). As pointed out in Applicants' "Response" to Office Action mailed April 16, 2003:

> The Wu reference cites variability of known RNase III proteins ***across animal species***, while the present invention discloses variability of the human RNase III polypeptide ***within the human species***. The **inter**species variability cited on page 36957, column 2, last paragraph of Wu (which states that "the human enzyme is distinctly different from the homologues in other species") describes RNase III **inter**specific homologues in other eukaryotes. **Inter**specific variablitiy is not equivalent to **intra**species variability observed within the genus of human RNase III polypeptides, much less to the limited variability present in polypeptides capable of cleaving double- stranded RNA or amino acid sequences having 90% sequence homology to SEQ ID NO:2, as claimed in claims 1 and 2, respectively. While **inter**species homology of the human RNase III protein of the invention is discussed in several parts of the present application (including page 6, lines 30-35, and page 7, lines 3-7, which describe a comparison of a human, RNase III amino acid sequence with RNase III amino acid sequences of other species) these other non-human species are not claimed -- Applicants claim ***human*** RNase III polypeptides. . . . [The ***maximum*** variation of species within the pending claims is 90%.] . . In stark contrast, in terms of **inter**species sequence homology, the closest RNase III to the human RNase III is in worm and shares only 41% sequence homology. . . Wu fails to support the Examiner's assertion that 'the species specifically disclosed are not representative of the genus because the genus is highly variant.'

For the foregoing reasons, Applicants respectfully request withdrawal of the written description rejection. Accordingly, reconsideration and withdrawal of this rejection is requested.

The examination of these claims and passage to allowance are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicant invites the Examiner to contact the undersigned at (215) 665-6904 to clarify any unresolved issues raised by this response.

Respectfully submitted,



Gwilym John Owen Attwell
Registration No. 45,449

Date: August 22, 2003
COZEN O'CONNOR, P.C.
1900 Market Street
Philadelphia, PA 19103-3508
Telephone: (215) 665-2000
Facsimile: (215) 701-2004

Attachments:
1) Elabashir *et al.* (Elbashir *et al.*, Nature 2001 15:188-200; "AD")
2) copy of initialed Form 1449 attached to the Office Action dated December 16, 2002 (paper no. 14).
3) Request for Corrected Filing Receipt
4) Unexecuted Oath/Declaration